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Space-time analysis and mapping of prevalence rate of tuberculosis in Ghana

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ABSTRACT

Background: Global fight against tuberculosis (TB) has received increasing attention over the years. However, the disease remains one of the top-most global health problems, especially in Sub-Saharan Africa and Ghana.

Aims: This paper examined geographical (regional) and seasonal distribution of TB cases providing relative risk of TB exposure in Ghana and step by step procedure to perform the analysis.

Methods and material: We modelled reported TB cases between 2015 and 2018 using wavelet analysis and applied maximum covariance analysis (MCA) to determine regional and seasonal patterns and the risk of TB exposure in Ghana. This study is based on the old administrative regions of Ghana.

Results: More TB cases were recorded in the Greater Accra and Ashanti regions and less cases in the rest of the regions. There is significant increase in the number of TB cases from 2015 to 2018. High number of TB cases is observed in the dry season relative to the rainy season. There is high variability in TB prevalence with high prevalence moving towards the Southern part of Ghana.

Conclusion: The study highlights that TB cases is clustered in space and time and that even at small spatial scale, differences in prevalence can be substantial. The prevelance of TB exposure is higher in the dry season relative to the rainy season. Hence, enough resources should be timely provided during the dry season as well as intensifying preventive strategies to control the spread of the disease.

Background

Research evidence indicates that tuberculosis (TB) remains a foremost global health problem that affects about 1/3 of the world's population. TB is one of the top 10 causes of death worldwide, and responsible for more deaths than HIV [1]. Despite research attesting to the global nature of the disease, empirical evidence suggests that TB is more prevalent amongst people

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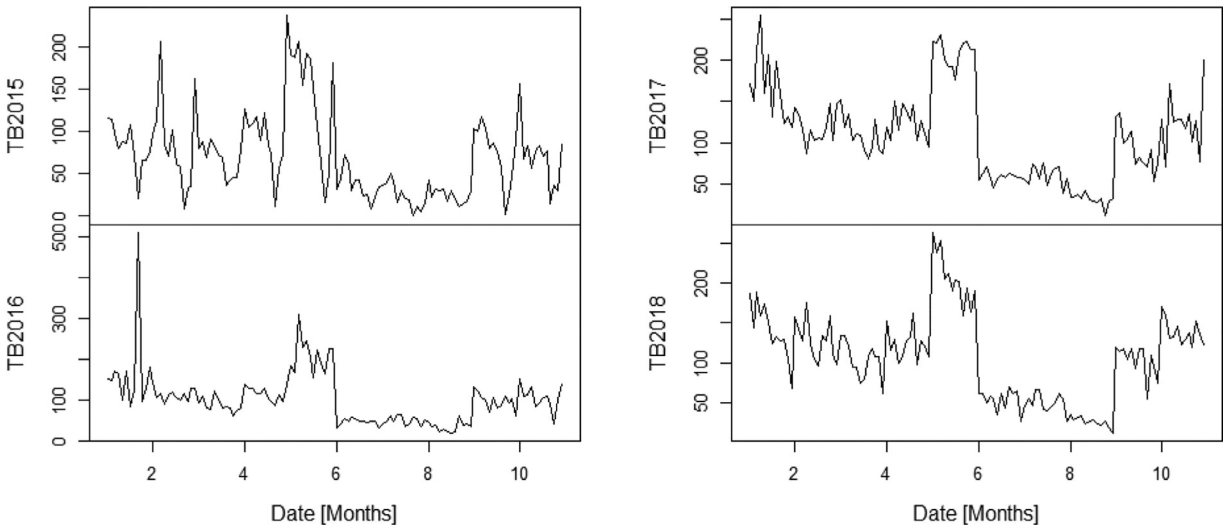

Fig. 1. Time series of tuberculosis cases plotted monthly.

Table 1
Counts of tuberculosis cases in 2015 and 2016 for the different regions in Ghana.

Year	Region	Mean	*N*	Std. deviation	Minimum	Maximum	Sum
2015	Ashanti	82.83	12	26.17	21	116	994
	Brong-Ahafo	86.25	12	56.2	8	207	1035
	Central	66.75	12	19.3	36	91	801
	Eastern	100.58	12	53.76	12	237	1207
	Greater Accra	140.75	12	64.88	17	207	1689
	Northern	37.08	12	17.6	9	73	445
	Upper East	24	12	15.6	0	50	288
	Upper West	25.08	12	9.03	11	42	301
	Volta	74.08	12	34.77	2	117	889
	Western	69.92	12	35.62	15	156	839
	Total	70.73	120	50.05	0	237	8488
2016	Ashanti	168.67	12	112.71	84	512	2024
	Brong-Ahafo	113.08	12	14.43139	91	140	1357
	Central	86.33	12	16.61	60	121	1036
	Eastern	115.1667	12	17.97	86	139	1382
	Greater Accra	209.92	12	43.26	153	310	2519
	Northern	45.42	12	8.31	30	56	545
	Upper East	49.42	12	10.82	34	64	593
	Upper West	33.75	12	12.08	19	61	405
	Volta	97.42	12	20.8	60	133	1169
	Western	105.42	12	28.57	42	152	1265
	Total	102.46	120	65.72	19	512	12,295

living in developing countries and it is a leading cause of morbidity and mortality [2,3]. Out of those infected globally, in Sub-Saharan Africa, over 1.5 million cases occur annually [4,5]. In Ghana alone, over 46,000 new tuberculosis cases are estimated by the World Health Organization annually [4]. The disease kills more adults each year than HIV, with women being the most affected.

The fight towards the eradication of TB globally has saved an estimated 54 million lives since the year 2000. The mortality rate has been reduced by 35 percent [1]. The World Health Organization (WHO) has a vision of decreasing TB deaths by 95 percent and decreasing the prevalence ratio by 90 percent by the year 2035 [1].

Mycobacterium, the organism that causes tuberculosis disease, has been present in the human population since 2400BC [6]. The organism spread through coughing, sneezing from someone already infected and repeated exposure to the organism may cause the disease [3,6]. The disease, is airborne with identified spatial autocorrelation in distribution at international, national, provincial and local levels during certain periods in time [3,6]. Various efforts have aimed at dipping the disease incidence and control its occurrence. This has been done through National TB control programmes and interventions as well as extensive studies to understand the dynamics of the disease. But there is paucity of studies on space-time modelling to describe the dynamics of the disease in Ghana.

Although there have been studies in Malaysia, Kenya, china and Ghana applying varying modelling methods to study the disease dynamics, little is known about applying this method to describe the seasonal and regional distribution of TB in

Table 2
Counts of tuberculosis cases in 2017 and 2018 for the different regions in Ghana.

Year	Region	Mean	*N*	Std. deviation	Minimum	Maximum	Sum
2017	Ashanti	168.25	12	42.3	118	255	2019
	Brong-Ahafo	118.83	12	19.95	87	148	1426
	Central	108.42	12	21.97	80	153	1301
	Eastern	123.5	12	19.2	94	151	1482
	Greater Accra	210.17	12	16.3	177	232	2522
	Northern	58.25	12	6.12	45	71	699
	Upper East	60.08	12	12.01	38	75	721
	Upper West	30.25	12	7.51	10	41	363
	Volta	92	12	25.93	52	137	1104
	Western	126	12	35.63	71	201	1512
	Total	109.58	120	55.76	10	255	13,149
2018	Ashanti	140.92	12	34.89	68	189	1691
	Brong-Ahafo	129.83	12	25.56	96	176	1558
	Central	103.25	12	22.89	62	135	1239
	Eastern	123.58	12	19.94	97	163	1483
	Greater Accra	206.17	12	32.03	159	264	2474
	Northern	53.92	12	12.93	27	69	647
	Upper East	49.75	12	11.5	27	66	597
	Upper West	25.83	12	6.45	12	35	310
	Volta	102.92	12	20.65	54	119	1235
	Western	138.33	12	16.18	120	171	1660
	Total	107.45	120	54.93	12	264	12,894

Table 3
One-way analysis of variance (ANOVA) and confidence intervals for TB cases for the various Years.

Groups	*N*	Mean	Std. deviation	S.E.	95% CI for Mean		*F*	*P*-value
					L	U		
2015	120	70.73	50.05	4.57	61.69	79.78	2.18	<0.001
2016	120	102.46	65.72	6	90.58	114.34		
2017	120	109.58	55.76	5.09	9950	119.65		
2018	120	107.45	54.93	5.01	97.52	117.38		
Total	480	97.55	58.86	2.69	92.28	102.83		

Ghana. The Malaysian study applied standardized morbidity ratio of TB and identified areas that had the lowest and highest risk of contracting TB. Two separate studies in Kenya identified best fit model for modelling TB relative risk and deduced that unstructured heterogeneity model performs better in terms of modelling and mapping TB relative risk. The authors observed that interaction of TB relative risk in space and time increased among rural counties which shared boundaries with urban counties that have high tuberculosis risk [7–9]. A study on the spatial and temporal clustering analysis of tuberculosis in China employed kulldorff's retrospective space time scan statistics, which helped them to identify twelve significant space time clusters of reported TB [3].

In Ghana, a mathematical model was developed to describe the dynamic behaviour of tuberculosis in the Northern part of Ghana. It was observed that the infection rate of tuberculosis is determined by the population of people living in the locality. Consequently, it was concluded that the higher the population density, the greater the risk of instability of the disease free equilibrium [6]. A study by Amo-Adjei and Awosabo-Asare [10] also indicated a rise in reported tuberculosis case in Ghana, from 43.6% to 87.7% between 1997 and 2010. Another significant observation made by the authors was that the rate of death was significantly more likely in the years 1998, 2003, 2005 and 2006 [10].

In another study, where the incidence of TB reported cases at a hospital in Ghana was estimated using the time series approach, no obvious increasing or decreasing trends were observed between the periods 2008 and 2017 [11]. Studying the spatio-temporal patterns of Tuberculosis in Ghana is necessary for the control and prevention of the disease. Many studies conducted have not examined spatio-temporal dimensions of TB disease in Ghana.

This study therefore focuses on space-time modelling of tuberculosis cases in Ghana to identify risk prone areas in the country, which may be helpful in timely allocation of resources and implementation of preventive strategies as well as guiding policy revision and formulation.

Methods

In this section, we introduce the study setting and the statistical methods used.

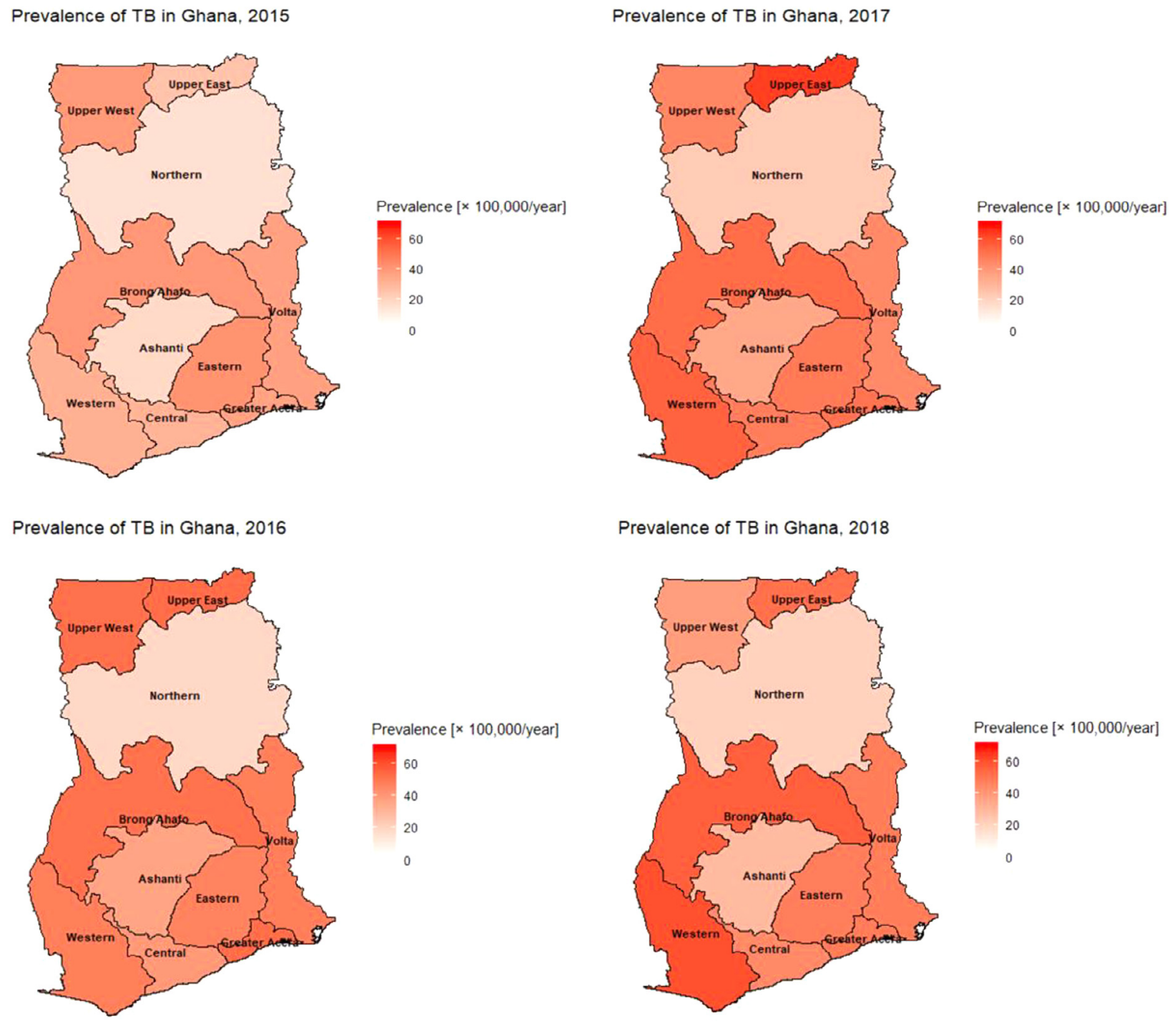

Fig. 2. Maps of prevalence of tuberculosis cases at regional level for the years 2015, 2016, 2017 and 2018.

Setting and data

Ghana is in the tropics and until December 2018, had ten [10] administrative regions; Namely, Northern, Western, Eastern, Central, Upper West, Upper East, Volta, Ashanti, Brong-Ahafo and Greater Accra. The country has two main climatic seasons: the wet and the dry seasons [4]. Northern Ghana (Northern, Upper East and Upper West) regions experiences their rainy season from April to mid-October while Southern Ghana (Volta, Ashanti, Brong-Ahafo and Eastern, Central, Greater Accra, Western) regions experiences their rainy season from March to mid-November [4]. In the southern part of Ghana, there is a bi-modal rainy seasons: April through June and September through November [5]. In this study we have modelled reported TB cases data generated from the Ghana Heath Services data gathering database (District Health Information Management System (DHIMS2)) considering those residents in these ten old administrative regions.

Ghana have a decentralized health system which operates at five levels: National, Regional, District, Sub- District and Community. Ghana Health Service (GHS) is authorized by Ministry of Health (MOH) to collect, collate and report on all routine health services including health service data from Mission, Private and Quasi-government health facilities everywhere in the country. GHS Collaborated with the University of Oslo to develop a software called the District Health Information Management System (DHIMS2). The database is centralized and allows easy, online updates. Health data is entered at the facility level only. Data can also be entered for a facility at the sub district or district level by only trained authorized persons. The database has a dashboard which can be customized to link different indicators to perform data quality analysis.

In this study, we generated data for reported TB cases between 2015 and 2018 from the DHIMS2 and used in the analysis. We also performed data quality checks and used data which fields were fully completed in the database and excluded all incomplete data and data which were extremely over reported than expected based on a standard expected case detection formula across regions.

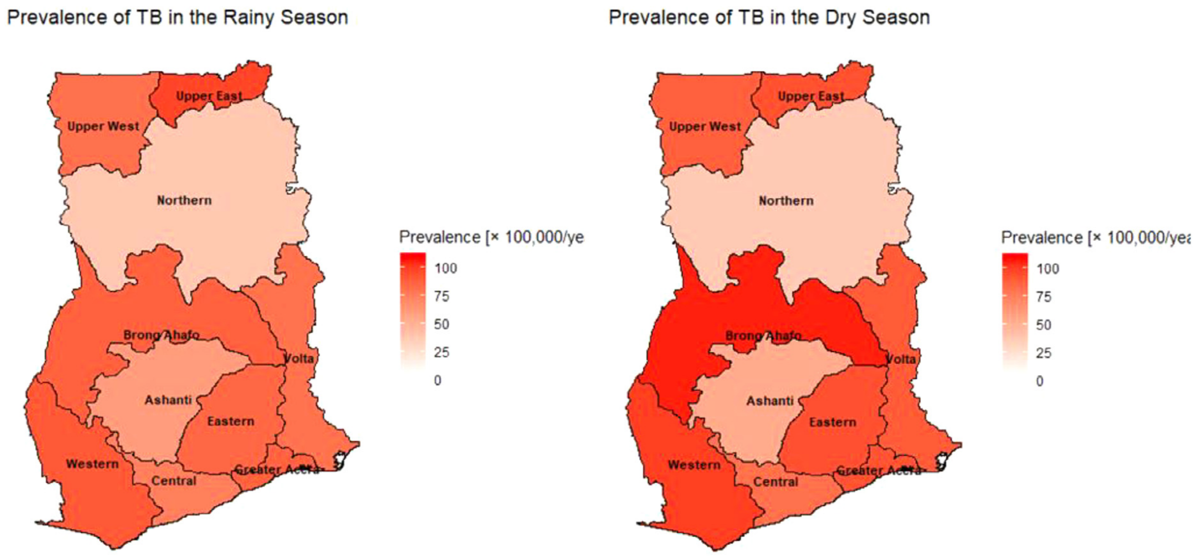

Fig. 3. Maps of seasonal prevalence of tuberculosis cases at the regional level.

Statistical analysis

In this section, we present and discuss the approach used to estimate and map prevalence rate (PR) of TB exposure in Ghana. We discuss spatial and spatio-temporal approaches for investigating spatial and spatio-temporal patterns of TB PR. These approaches allowed us to carry out spatio-temporal analysis of reported TB cases in Ghana. Also, the approaches allowed us scan for spatial clusters on yearly and regional basis of the disease.

Prevalence rate

Here we focused on constructing yearly prevalence maps at different levels of spatial resolution and to present a map at the regional levels across seasons (rainy and dry seasons). We also focused on identifying areas associated with higher risk of TB prevalence. We computed the prevalence as follows [12]:

Let n_{ij} denotes the number of TB cases and P_{ij} denotes the total population at time j within a region i. It follows that the prevalence rate (PR) can be calculated as

$$PR_{ij} = \frac{n_{ij}}{P_{ij}} \tag{2.1}$$

To have information on the seasonal pattern of the spatial distribution of TB prevalence, we further estimated, for each season of the year and averaged them over the years being studied. We estimated the seasonal prevalence using the standard Ghana population associated with each study period. We then built the regional prevalence maps by collapsing the data from the district level to regional level. This study considered the 10 old administrative regions of Ghana including Northern, Western, Eastern, Central, Upper West, Upper East, Volta, Ashanti, Brong-Ahafo and Greater Accra. In this paper, we build the prevalence maps using the R package Map tools for reading geographic data [13–17].

Wavelet analysis

Although methods such as the SaTScan software can be used to detect temporal and spatio-temporal clusters, this method in principle is not suitable for time series that are non-stationary which is often the case for many epidemiological and ecological data [18,19]. The graphical display of the TB data in Fig. 1 gives an indication that these data are non-stationary. Therefore, for the temporal or spatio-temporal analysis, we used wavelet analysis instead of the spatial scan statistic which is specifically suitable for non-stationary time series data. We compared the temporal patterns of the reported cases of TB at spatial scales by using the ten old administrative regions of Ghana.

The wavelet analysis uses a local periodic function (the wavelet) to decompose fluctuations of time series observed during a small stretch of time into a series of different periodicities. Given the relative importance of periodicities (wavelet power) contour plots are then plotted as a function of time. This provides a tool for both the periodicity, and the timing of the fluctuations to be monitored. More detailed information on wavelet analysis can be found in [12,18–25].

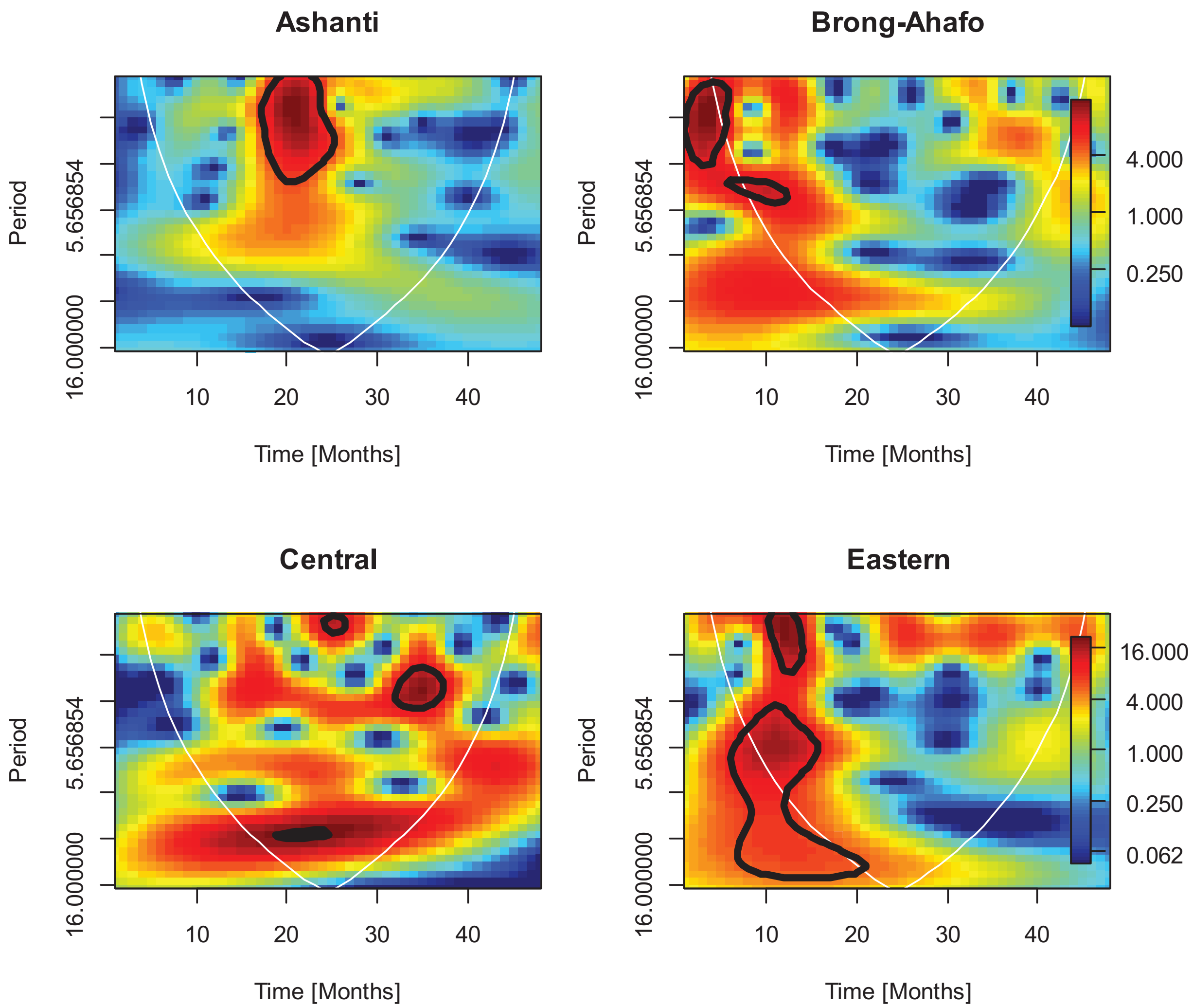

Fig. 4. Wavelet power spectra of tuberculosis prevalence for Ashanti, Brong-Ahafo, Central and Eastern regions of Ghana. *Colour codes represent wavelet power and areas inside the black contour lines correspond to 95% confidence regions where the power is higher than the power of red noise with the same autocorrelation coefficient as the data. Transparent areas on the left- and right-hand sides of the plots represent the cone of influence, which is a region where edge effects are important.*

To capture and explain the differences in the temporal dynamics of TB at the spatial scale, observing that TB data was non-stationary we applied wavelet cluster analysis to the time series of reported TB cases of all the ten old administrative regions of Ghana.

Wavelet cluster analysis

Given the wavelet spectra of the different regions, we then quantified the similarity between the patterns using a Maximum Covariance Analysis (MCA). This approach produced dissimilarity matrix of the wavelets [23,24] which is subsequently used to construct a cluster tree based on the Ward's agglomeration criterion. Further information on wavelet clustering and its application in ecological and epidemiological studies can be found in [23,24,26,27]. In this paper, the wavelet spectra and the wavelet cluster tree have been computed using the R package "biwavelet" [13–17].

Results

TB cases seem to be higher in more populated regions of the country. For instance, the Greater Accra region which is the most populous region in the country recorded the highest cases of TB in all four years (Tables 1 and 2). However, in 2015, the Ashanti region which is the 2nd most populated region in the country after Greater Accra region recorded less TB cases

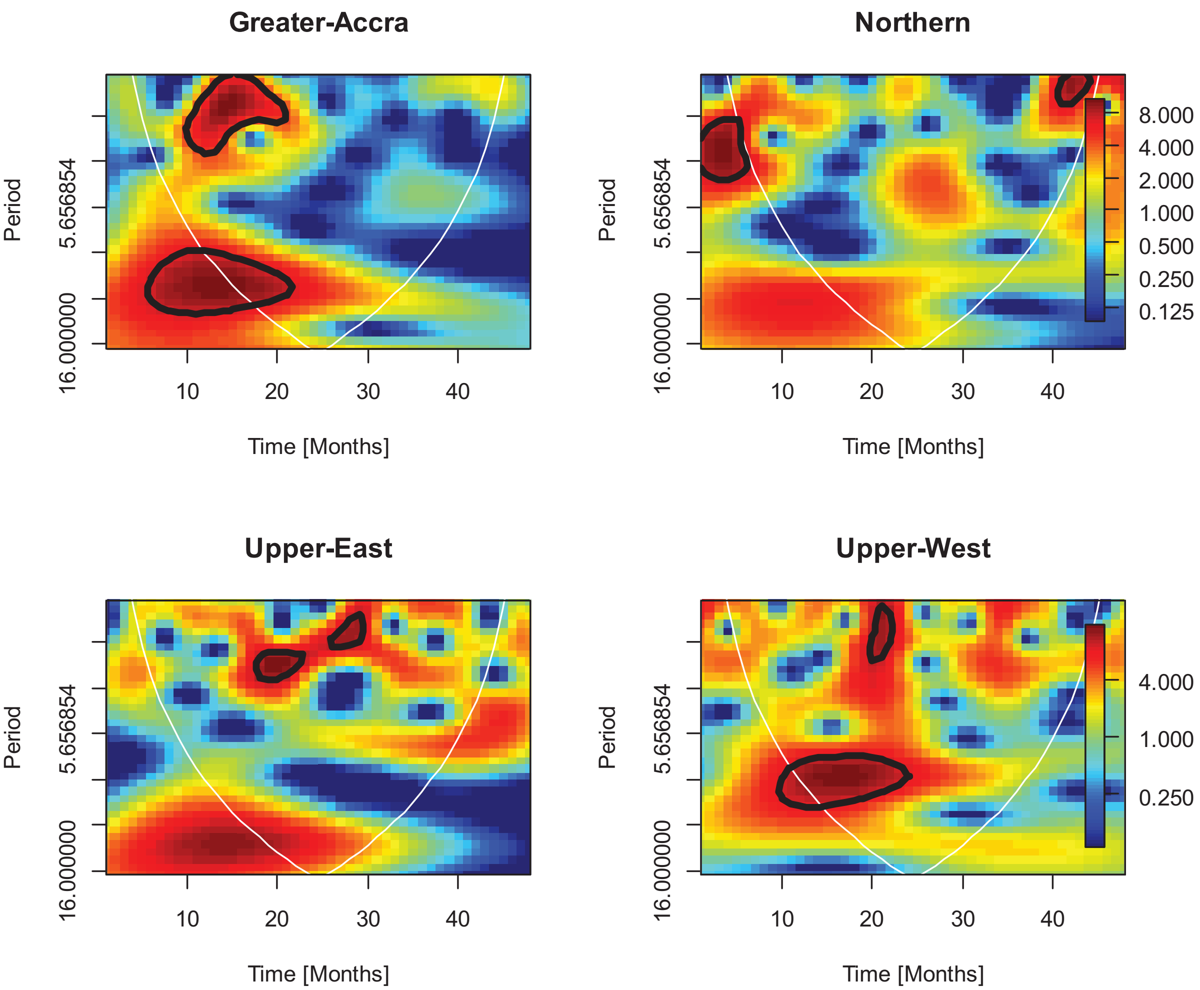

Fig. 5. Wavelet power spectra of tuberculosis prevalence for Greater-Accra, Northern, Upper-East and Upper-West regions of Ghana.

than some of the regions that are comparatively less populated such as Brong-Ahafo, Eastern, Volta, and Western Regions (Table 1).

Furthermore, the average number of TB cases in 2015 is significantly lower than in 2016, 2017 and in 2018 (One-way ANOVA, p-value$<$0.001). It can also be stated with 95% confidence that the average number of TB cases for the whole country over the study period is between 92 and 103 (see Table 3).

We observed that the temporal dynamics of TB cases display a strong seasonal pattern with peaks in the dry season and troughs in the rainy season (Fig. 1). This seasonal oscillatory behaviour is observed in all years, although the difference in number of TB cases between dry and rainy seasons is more pronounced in 2016 and 2017.

The prevalence of TB is heterogeneously distributed across the country (Fig. 2). A zone of high prevalence stretches from north to south (redder colours in the maps in Fig. 2). Differences between low-versus high-prevalence regions are consistently more than one order of magnitude. In fact, in the yearly maps (Fig. 2), the prevalence in the dark red areas ranges from 40 to 70 per 100,000 per year, while the prevalence in the white areas ranges from 0 to 20 per 100,000 per year.

The seasonal maps are presented in Fig. 3, where we observed that the contrast between high and low prevalence areas is also remarkable. Even in rainy season, when prevalence is much lower, low and high prevalence values differ by more than one order of magnitude: some regions (white areas) are characterized by an average prevalence of 38 to 60 cases per 100,000 per year, and others (dark red areas) by an average prevalence 70 to 107 cases per 100,000 per year. The temporal dynamics of TB is characterized by higher values in the dry season and relatively lower values in the rainy season in all 10 regions.

We were also interested in capturing differences in the temporal dynamics of TB at the spatial scale. Because of the non-stationarity of the data, we applied wavelet cluster analysis (see Methods) to the time series of TB cases of all ten regions of Ghana. Wavelet spectra revealed a significant periodicity of about 12 months (red areas inside the black lines) in the

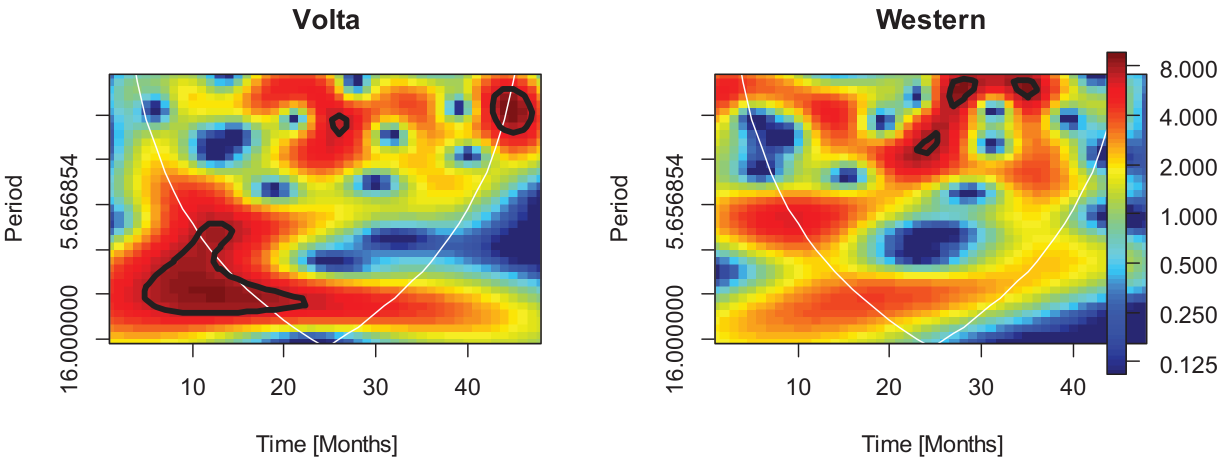

Fig. 6. Wavelet power spectra of tuberculosis prevalence for Volta and Western regions of Ghana.

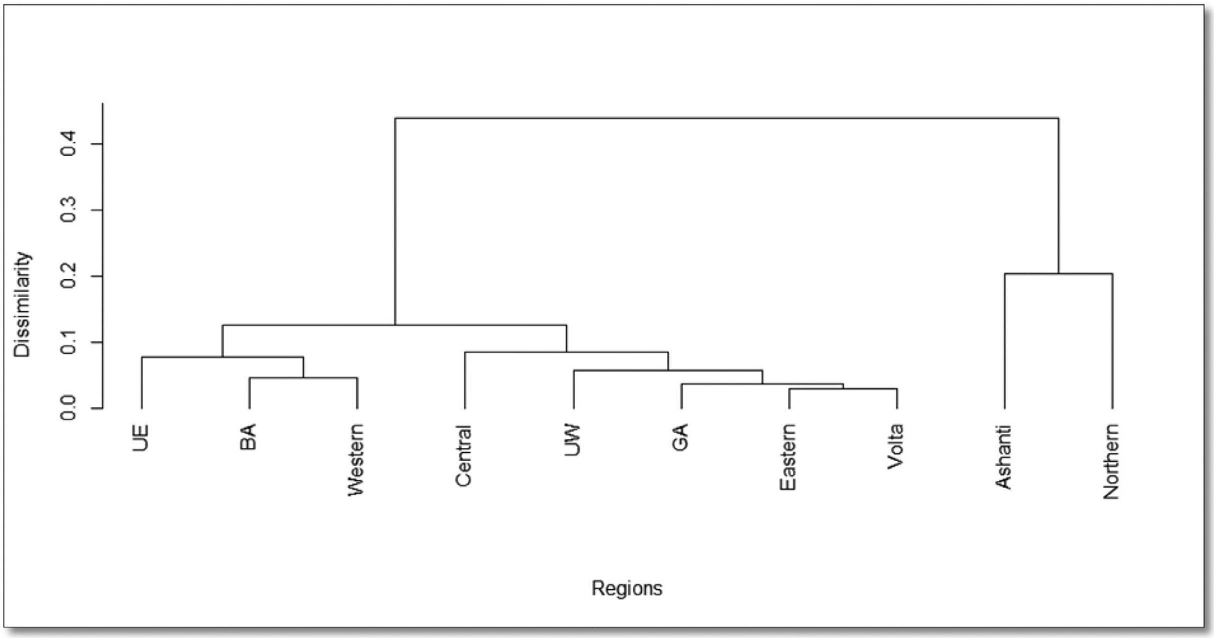

Fig. 7. Cluster dendrogram for tuberculosis cases in Ghana based on the dissimilarity matrix of the wavelets power spectra.

Eastern, Greater Accra, Upper-West, and Volta regions (Figs. 4, 5, and 6). For the Brong-Ahafo, Central, Northern, Upper-East, and Western regions; wavelet analysis identifies a significant periodicity of only about 1 to 2 months (Figs. 4, 5, and 6). In the time lag between the 7th month of 2016 and 2nd month of 2017, wavelet analysis identifies a significant periodicity of about 4 months for Ashanti region (Fig. 4). This coincides with the peaks of TB cases occurring at the beginning of 2017 (see Fig. 1).

We also built a tree based on a wavelet dissimilarity matrix (Fig. 7). The dissimilarity matrix identifies three levels of aggregation. At the left side we have Upper-East, Brong-Ahafo, and Western regions clustered together as high. In the middle, we have Central, Upper-West, Greater Accra, Eastern, and Volta regions clustered together as medium. Ashanti and Northern regions are clustered together at the right side as low. Strikingly, the partition detected by the cluster analysis coincides with the partition of high and low prevalence areas observed in the prevalence maps (Fig. 2).

Conclusions

Tuberculosis (TB) prevalence remains one of the top-most global health problems and the prevalence is more pronounced in Sub-Saharan Africa and also a concern to Ghana. The need to study spatio-temporal patterns of the disease in Ghana to make informed decisions in the control and preventive effort is imperative. In this paper we model/estimate and mapped prevalence rate of TB in Ghana. We applied wavelet analysis and wavelet cluster analysis to study the space-time (regional and seasonal) patterns of TB prevalence rate in Ghana.

The study revealed that Greater Accra region consistently has the highest mean TB cases over the study period and there is a general increase in the mean TB cases in this region with a very slight reduction in 2018. Although the mean TB cases for Ashanti region is the lowest when compared with Brong-Ahafo and Eastern regions in (2015), Ashanti region is the second region after (Greater Accra region) with the highest mean TB cases in Ghana. Also, Greater Accra region is the region with the highest population density in Ghana followed by the Ashanti region, which probably accounts for the larger numbers of TB cases in the Greater Accra and Ashanti regions. Further, Upper West region has the lowest mean TB cases relative to all the regions in Ghana, probably due to low population density in this region. The summary statistics suggests lower mean TB cases in the Northern zone (Northern, Upper West, and Upper East regions) relative to the other zones.

The results showed that the mean TB cases in 2015 is significantly lower compared with the years 2016, 2017, and 2018. The average number of TB cases in 2015 is significantly (p-value$<$0.05) lower than in 2016, 2017 and in 2018. Using the 95% confidence intervals (95% CI), it is observed that there is an overlap among the 95% CIs for 2016, 2017, and 2018 except for the year 2015. This gives an indication that there is higher variability in the mean TB cases in 2015 (95% CI = 62–80) and the other years (95% CI = 91–120).

The TB evolution shows seasonal pattern with high peaks observed in the dry seasons and low peaks in the rainy seasons. This behaviour in the seasonal pattern of the TB cases is observed in all the years. However, this is remarkably high in 2016 and 2017.

The maps of TB prevalence from 2015 to 2018 showed that there is variability in TB prevalence among the 10 regions of Ghana. In general, there is variability in TB prevalence over the study period with high prevalence moving towards the Southern part of Ghana. Also, the seasonal (rainy and dry) maps of the TB cases showed that there are more TB cases in the dry season relative to the rainy seasons. This gives an indication that more TB cases are likely to be recorded in the dry season compared with the rainy season. The ease at which TB mycobacterium can travel in air (with much air blowing in the dry season) probably accounts for the high TB prevalence observed in the dry season.

Declarations of Competing Interest

The authors declare that they do have any conflict of interest.

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Author contributions

All the authors carried out the literature review. SA wrote the background, AI wrote the methodology and the discussion and conclusion, and WI performed the statistical analysis and interpretation of the results. All the authors reviewed, proofread, and provided comments on the results. All the authors have read and approved the final version of the manuscript.

Ethics and consent

N/A.

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